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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,196	ALLEN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8,9 and 35-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8,9 and 35-47* is/are rejected.

7)☒ Claim(s) *9 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed 02/11/2005 has been received. Claims 1-5,7 and 10-34 have been cancelled. Claims 6,8 and 42-47 have been amended. Claims 6,8,9 and 35-47 are pending and under consideration ion the instant office action.

Specification

The amendment filed 02/11/2005 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

Applicant has amended the specification at page 12, paragraph 4 to incorporate US Provisional Application 60/084194. This reference is not considered new matter because the original specification incorporated USSN 08/971310 by reference, which was converted to the Provisional Application 60/084194. However, the additional references are considered new matter. The references include a second provisional application (60/084949), a utility application claiming priority to the two provisional applications (09/193,834) and a second utility application that is a continuation of the first utility application (09/885,816; published as US Patent 6,815,185). This incorporation by reference adds new matter to the specification.

Claim Objections

The objection to claim 6 is withdrawn in light of Applicant's amendment to the claim.

Applicant has traversed the objection of claim 9 regarding the recitation that a pseudopregnant mouse gives birth. Applicant refers to a published textbook setting using the terminology and asserts that the terminology would be clearly understood by one skilled in the art (see page 5, paragraph 4 of Applicant's Remarks). In response, the objection is maintained.

Upon impregnation, the pseudopregnant mouse of the claim is no longer pseudopregnant. The clarity of references to pseudopregnant mice in a textbook has little weight in establishing that it is accepted in the art to call a pregnant mouse pseudopregnant. For the sake of clarity, Applicant should amend the claim to read "wherein the resulting pregnant mouse gives birth to a chimeric mouse".

Claim 43 is objected to because of the following informalities: The term "endogenous" is misspelled in line 1.

Appropriate correction is required.

Claim 45 is objected to because of the following informalities: The claim refers to a "selection marker"; however, the specification refers to a "selectable marker" (see page 15, line 14, for example).

Appropriate correction is required.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Utility

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

See also the MPEP § 2107 - 2107.02.

Claims 6,8,9 and 35-47 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The rejection set forth on pages 2-6 of the previous office action mailed 11/12/2004 is maintained for reasons of record.

The instant specification has discussed that the mice of the instant invention can be used as models of disease to screen for drug therapies. Applicant has also argued that the mice of the invention can be used as a tool for studying the function of an FPR-RS4 gene (see page 5, paragraph 2 of Applicant's Remarks filed 08/31/2004. As set forth in the previous office action, these uses fail to meet the standards of a specific, substantial and well-established utility required

under 35 U.S.C. 101. In summary, the utilities asserted in the specification by Applicant for the claimed mouse are not specific or substantial and therefore are not well established because the use of the mouse in screening for drugs to treat an unknown disease is not specific. The basis for this rejection is further set forth in the previous office action and in the guidelines above.

Applicant's arguments filed 02/11/2005 have been fully considered but they are not persuasive.

Applicant argues that the Patent Office guidelines state that an asserted utility should be presumed to be true (pages 6-7). Applicant asserts that the well-known use of the claimed mouse is in characterizing the function of the FPR-RS4 gene. Applicant cites excerpts from an NIH website, Austin et al., Lewin, Joyner, Matise and Albert's Molecular Biology of the Cell in establishing that knockout mice are invaluable tools of scientific research (pages 8-10). Applicant also cites the MPEP in discussing the utility of research tools (page 9 of Applicant's response; MPEP 2107.01, I). In general, Applicant does not understand how the invention cannot have utility when the invention is being used by one of skill in the art and has clearly been accepted as useful by several leaders in the field of transgenic technology.

In response, the instant invention has failed to meet the requirements of possessing a well-established utility and for a use with any particular practical purpose. A well-established utility and a utility with a particular practical purpose is one that is specific and substantial (see MPEP 2107(II)(A)(3)(ii) and MPEP 2107 (II)(B)(1)). The utility of the instant invention is neither specific nor substantial for reasons of record. Applicant is reminded that the utility guidelines (see above) expressly state that utilities requiring further research to identify or reasonably confirm a use do not define substantial utilities. Examples of uses that are not

considered substantial utilities include basic research in studying the claimed product and use to screen for therapeutics for an unspecified disease. The use of the invention by the skilled artisan does not impart patentability or patentable use on the invention for reasons set forth above.

With specific respect to Applicant's applied references, the validity of the opinion of the NIH and Bruce Albert with respect to the value of the knockout mouse in determining gene function is not questioned. However, the use of a mouse to determine gene function, as set forth above, does not meet the requirement that a utility be specific and substantial, and therefore, does not fulfill the requirements of utility under 35 USC 101. With respect to MPEP 2107.01, I, a gas chromatograph is a research tool with a well-defined function and highly specific use that does not necessitate further study of itself. It may be that a gas chromatograph may be used for a wide variety of analyses of other products; however, this does not change its specific use for analyzing a sample. In contrast, the claimed invention is not a general tool for analyzing other samples and, at most, serves to study the function or characteristics of itself. In this respect, the utility of a knockout mouse cannot be compared to a gas chromatograph. Therefore, the utility of the instant invention is neither specific nor substantial.

Applicant also discloses the commercial use of the claimed mice and states that commercial use and acceptance is one important indication that the utility of an invention has been recognized by one of skill in the art (page 11 of Applicant's remarks). Applicant states that they are willing to submit an affidavit as evidence of the sale of the mouse.

In response, Applicant fails to provide description or evidence of such commercial use. Applicant has not provided any evidence that the mouse was purchased or why the mouse was purchased. Because no evidence is provided as to why the mouse was purchased, the relevance

of the sale of the mouse to its utility is unclear. The commercial use of the claimed mouse is not dispositive of the lack of a specific and substantial asserted utility in the original specification and does not provide evidence of a well-established use. As set forth above and in the previous office action, theses uses are not specific or substantial. Applicant is reminded that the requirements under §101 and §112, 1st para. must be met at the time the application is filed. The discovery of a use meeting these requirements after the application is filed does not satisfy the statutory requirements under either §101 or §112, 1st para. See *In re Kirk*, 153 USPQ 48, 52 (CCPA 1967); *In re Wright*, 27 USPQ2d 1510, 1514 (Fed. Cir. 1993).

Applicant argues that the examiner is maintaining contradictory positions in asserting that one of ordinary skill in the art would have been sufficiently motivated to disrupt the FPR-RS4 gene to determine its role in relation to other FPR genes and that the mouse lacks patentable utility (see page 11, paragraph 4 of Applicant's Remarks). Applicant asserts that the use of the claimed mouse to determine its role in relation to other FPR genes is specific and substantial.

In response, the positions Applicant is referring to as contradictory are based under entirely different statutes. The claimed invention is held to not have patentable utility under 35 USC 101 because the asserted utility of the mice is not specific or substantial. The claimed invention is held to be obvious under 35 USC 103(a) and such a rejection does not impart patentable utility on the invention. There is no requirement under 35 USC 103(a) that an invention have patentable utility to be obvious.

Applicant has referred to the principles set forth in *In re Brana* (see pages 12-17 of Applicant's remarks). Applicant asserts that the specification supports a use of the knockout mouse that is specific and substantial in light of the teaching of *In re Brana*.

In response, the fact pattern in *Brana* does not correlate to the fact pattern of the instant application. In *Brana*, the court addressed two separate issues, utility and enablement. The court held that the specification did, in fact, disclose a specific and substantial use for the compound, treating leukemia, and that this use was overlooked by the PTO in making the rejection under 101. The court observed that the claimed compound was similar in structure to compounds in the prior art that were useful in treating leukemia. The claimed compound behaved in a manner similar to that of the prior art in art accepted assays for anti-leukemic activity. Therefore, the specification enabled the use. The instant specification and the art of record fail to support such a patentable utility for the instant invention and therefore, the principles set forth in *In re Brana* do not apply to the instant invention.

Applicant asserts that an association between the FPR-RS4 gene and increased anxiety, decreased coordination, impaired balance and decreased susceptibility has been made (page 15, paragraph 4). Applicant appears to be setting forth that no further experimentation is needed for the skilled artisan to know how to use the claimed mouse. As set forth on pages 3-5 of the office action mailed 09/10/2003, a nexus between the FPR-RS4 gene and any of the disorders has not been clearly established. Further research is required to reasonably confirm such a link. First, there is no evidence of record indicating a role for FPR-RS4 in any of the disorders listed above. Second, the evidence provided in the specification is not conclusive and fails to overcome the art-accepted caveats in establishing a link between gene knockouts and behavioral phenotypes. There are several sources of unpredictability in assessing the phenotype of knockout mice that have been documented in the art raising doubt to correlation of the phenotype of a specific knockout mouse to the gene disruption per-se. The laboratory environment in which the mice are

kept and studied may have an effect on observed behavioral phenotypes. The difference in degree of many behavioral phenotypes between mice of different genetic backgrounds can differ between laboratories [Crabbe et al., **Science** 284: 1670-1672, 1999). Furthermore, it is widely recognized that the different inbred strains of mice commonly used to make knockout mice vary widely in behavioral characteristics. As a result, the specific genetic background of the strains of mice used to create a knockout mouse can be responsible for or contribute to a phenotype observed in the knockout mouse. For example, Crawley [1997, **Psychopharmacology** 132 (2): 107-124, specifically page 108, col. 1] discloses that both 129 Ola and C57BL/6 are unusual in many behavioral paradigms including those disclosed in the instant invention. Gerlai [1996, **Trends in Neurosci.** 19 (5): 177-181, specifically page 179, col. 1) discloses that 129 mice display a variety of differences in behavior compared to other inbred mouse lines, including in performance in a rotorod test. Bampton [1999, **Brain Res.** 841 (1-2): 123-134, specifically page 124, col. 1] teaches that the combination of 129 Ola and C57BL/6, used by applicant, is particularly problematic due to their differences in genetic background and observed phenotypes that may be a result of combining the two genetic backgrounds. Further issues complicating the association of a phenotype with a gene-knockout and correlating gene function to the gene is set forth by Crawley [**Trends in Neuroscience**, 19:181-182, 1996]. Therefore, the skilled artisan would necessarily have to perform additional characterization of the claimed to reasonably confirm that the claimed mice actually have any of the claimed phenotypes as a result of the claimed gene disruption and to reasonably confirm that the claimed mice have a real-world use. Additional experimentation, such as making the claimed mice in additional genetic backgrounds

or by additional phenotypic tests to confirm the observed phenotypes that have been correlated unduly to diseases or disorders, is necessary to confirm a real world use.

Applicant has stated that the mice are useful for studying expression of the FPR-RS4 gene because the mice contain a lacZ reporter gene (page 18 of Applicant's response). Claim 6 has been amended to recite that the mouse contains a null allele that comprises exogenous DNA. Claim 46 recites that the exogenous DNA encodes a visible marker. Claim 47 recites that the visible marker is lacZ.

In response, this is only a general utility of further research that applies to any knockout mouse comprising a lacZ gene in the targeting construct and is not specific. It is a widely used technique to generate mouse knockouts by inserting a visible reporter gene into an endogenous gene. Characterization of the lacZ expression pattern merely amounts to further characterization of the mouse itself and does not establish a real-world use for the mouse. Furthermore, the art of record has established that the endogenous FPR-RS4 gene does not appear to be expressed in mice and is not present in the genome of humans (Gao, 1998, Genomics, 51:270-276; specifically Abstract, page 274, col. 2, lines 1-2). Thus, it is not clear that any lacZ expression observed would be indicative of the endogenous expression pattern of FPR-RS4 in mice and is not correlatable to anything in humans. Additionally, the instant specification teaches that slight lacZ expression was detected in the testis. If this expression pattern were to be indicative of the expression pattern of the endogenous FPR-RS4, then it raises further question to the correlation between the FPR-RS4 gene, expressed only in the testes, and behavior such as anxiety, susceptibility to seizure and balance because it is not known how expression of a gene in the

testes can affect such diverse and numerous behaviors. It is noted that neither the endogenous nor the lacZ of the instant invention are expressed in the nervous system.

In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse and cells encompassed by the claims to be specific and substantial.

Enablement

Claims 6,8,9 and 35-47 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The rejection of claims 6,8,9 and 35-47 as presenting further issues of enablement is maintained for reasons of record as reiterated below and (see pages 6-9 of the previous office action).

Applicant's arguments filed 02/11/2005 have been fully considered but they are not persuasive as they relate to the enablement rejection based on the lack of utility of the claimed mice. However, arguments pertaining to other aspects of the enablement rejection are partially persuasive as set forth below.

1) Claims 6,9,40,41,43-47 were previously rejected as not being enabled because the claims fail to recite a phenotype for the mouse and therefore the claims encompass a mouse whose genome comprises a disruption of the FPR-RS4 gene wherein the mouse exhibits any phenotype, including wild-type.

Applicant has argued that the claims contain the structural and functional limitation that the FPR-RS4 allele is a "null" and that any phenotypes associated with the heterozygous and

homozygous null mice are inherent (page 19, last 2 paragraphs). Applicant argues that the unpredictability of phenotype as set forth in the art is related to predictability of phenotype a priori and that this unpredictability is overcome given the teachings of the specification (page 20).

In response, first, phenotypic limitations from the specification cannot be read into the claims. Second, the phenotype of the mice broadly encompassed by the claims is not predictable based on the guidance and teachings provided by the specification. While in Applicant's laboratory, a number of behavioral phenotypes were observed in some number of knockout mice that were generated using 129/OlaHsd ES cells followed by breeding to C57BL/6 mice. Mice of different genetic backgrounds were not made. As set forth in the previous office action mailed 09/10/2003, behavioral phenotypes can be drastically affected by genetic background and often times a behavioral phenotype observed in knockout mice is a result of the combination of genetic backgrounds (for example, see Belzung, 2001). It is also noted in the art for other non-behavioral phenotypes, that genetic background can have huge and misleading effects. For example, disruption of the mouse CF-1 leads to loss of embryos around the time of implantation in one strain and survival until the third week post-birth in another strain [Pearson, 2002, **Nature**, 415:8-9, specifically page 8, col. 2]. Consequently Silva et al., [1997, **Neuron**, 19:755-759] suggests making knockout mice using multiple genetic backgrounds. Silva also notes that 129 strain ES cells is not the best choice, however, backcrossing can be used to derive congenic mutant lines. It is noted that the instantly claimed mice were generated using a 129 strain of ES cells and only a single backcross was performed (page 53, lines 25-29) followed by inbreeding, which, according to Silva et al, should be avoided (page 756, col. 1, lines 8-12). Silva also

teaches that WT littermates are not the best controls (see legend, Figure 3). Silva et al continues in teaching

"...each study should be evaluated for its own merits and in the context of other available information. For example, the nature of the experimental question, the known variability of the phenotype tested, and the natural range of phenotypes found among related non-mutant lines all can affect the impact that genetic background may have on the interpretation of the results. Clearly, a subtle behavioral phenotype resulting from a mutation of a poorly characterized gene should be interpreted with great caution" (paragraph bridging pages 758-759).

With respect to the instant invention, Crabbe has taught that a large number of behavioral tests are greatly affected by genetic background and results can further vary greatly based on laboratory environment characteristics that are difficult to control (see paragraph bridging pages 1670-1671). Furthermore, Gao demonstrates the poorly characterized nature of the FPR-RS4 gene in mice, as expression of the gene is not even detectable or demonstrable. Therefore, the advice of Silva et al. clearly applies to the instant invention and should be heeded as the instantly claimed mouse involves a poorly characterized gene, phenotypes known to be greatly affected by genetic background and known to be widely variable.

Therefore, in light of the teachings in the art that genetic background has great effect on phenotypic manifestations of a gene disruption, that WT littermates are not the best controls and that there is great variability in behavioral testing outcomes based on environment, the teachings provided in the specification fail to definitively correlate the observed phenotypes with the claimed gene disruption in mice. The claims broadly encompass any phenotype, including wild-type, and including the phenotypes reported in the specification as well as any other phenotype. Accordingly, it cannot be assumed that any null FPR-RS4 mutant mouse will exhibit the phenotypes taught in the specification and those phenotypic limitations cannot be read into the

claims. The "null" limitation recited in the claims is, therefore, not sufficient to overcome the unpredictability of phenotype set forth in the art.

2) The aspect of the rejection with respect to the specification enabling a null allele is withdrawn.

3) The aspect of the rejection relating to the presence of SEQ ID NO:1 in the genome of the mouse (claim 43) is withdrawn in light of Applicant's amendment to the claim. However, the amendment necessitates the following new grounds of rejection.

4) Claim 43 has been amended to recite that the FPR-RS4 allele encodes mRNA comprising the sequence of SEQ ID NO:1. The mRNA encoded by the FPR-RS4 does not comprise SEQ ID NO:1. SEQ ID NO:1 is a DNA sequence and not an mRNA sequence. mRNA is made of different nucleic acids, namely uracil in place of thymidine. Therefore, the skilled artisan would not know how to disrupt a gene encoding an mRNA with thymidine residues in place of uracil because cells naturally make mRNA using uracil, not thymidine. Furthermore, the specification has not demonstrated that the FPR-RS4 gene is translated into mRNA.

New Matter

Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 43 contains new matter as it recites "mRNA". There is no literal support for this terminology in the specification. There is no disclosure of an mRNA and no evidence that this gene is expressed to make an mRNA.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 6,8,9,40,41 and 43-47 under 35 U.S.C. 103(a) as being unpatentable over Mansour in view of Gao is maintained for reasons of record set forth on paged 10-11 of the previous office action.

Applicant's arguments filed 02/11/2005 have been fully considered but they are not persuasive.

Applicant argues that if one of skill in the art would not know how to use the invention, as established by the rejections under 35 USC 101 and 112, first paragraph, then it is questioned how one can be motivated to make the invention. Applicant also questions how it can be argued that the specification fails to teach how to make the claimed invention when it is stated in the office action mailed 11/12/2004 that it was routine in the art to knockout genes (page 22, paragraph 2).

In response, first, it is not required under 35 USC 103(a) that the prior art have a patentable utility. Much of basic research does not meet the requirements of 35 USC 101. Clearly, this research is useful and is carried out by scientists. The distinction that basic research is useful to

scientists but does not meet the standards of utility set forth by 35 USC 101 is set forth in *Brenner v. Manson*, [148 USPQ 689 (US SupCt. 1966)]. Therefore, a claimed invention can be rejected concomitantly under 35 USC 103(a) and 35 USC 101. Second, the aspect of the enablement rejection with respect to making the claimed invention is with respect to the breadth of the claims. The claims encompass the mouse that is made obvious by Mansour and Gao, however, it comprises further embodiments that are not enabled. Furthermore, enablement requires an enabling disclosure for both how to make and how to use. 35 USC 103 does not require that the prior art teach how to use a product. Thus, a claimed invention can be rejected concomitantly under 35 USC 112, 1st paragraph as lacking enablement and 35 USC 103(a).

Applicant argues that a proper analysis under 35 USC 103 requires consideration of the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition and whether the prior art would also have revealed that in so making, those of ordinary skill in the art would have a reasonable expectation of success. Applicant argues that neither factor is satisfied by the prior art. Applicant asserts that only the FPR-RS4 cDNA is known and that Mansour teaches using genomic sequence in making a targeting vector.

In response, the DNA taught by Gao and listed in Genbank (Accession #AF071182) is, in fact a genomic DNA. All of the information necessary to make a null, knockout FPR-RS4 mouse as encompassed by the claims was known at the time of filing and taught by Mansour and by Gao. Gao does teach the genomic DNA sequence for the FPR-RS4 gene by referencing the Genbank Accession number, which was publicly available at the time of filing. One would have a reasonable expectation of success in making the claimed mouse because it was routine in the art at the time of filing to create a gene targeted mouse, using any region of the gene, including

coding and non-coding regions. There are no phenotypic limitations in the rejected claims or any other limitations that are not met by the teachings of Mansour and Gao.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER